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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,796	04/21/2006	John S. Debenham	21176Yp	5856

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EXAMINER	
DESAL, RITA J	

ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,796	DEBENHAM ET AL.	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *8-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 13* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/8/07; 6/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12 are pending.

Applicants have elected Group I of the restriction claims 1-7 and 13 wherein Ar1 and Ar 2 are phenyls, R3 is a H.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 13 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for some substitutents such as R1 to be –C=OCH3, alkyl, halogens, R2 to be and alkyl or NR5R6, R5, R6 to be H, alkyl, CO2Rc and some other variable as given by the examples in the table , R4 to be an alkyl or an alkyl aryl, does not reasonably provide enablement for all the various substitutents such as the heteroaryl , cycloheteroalkyl, cycloalkyl and so on.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds from an aromatic carbocyclic moiety to an aromatic carbocyclic moiety having many large electron withdrawing and bulky groups substituted on it to a moiety having many heterocyclic rings. These compounds cover a very wide range of compounds. The various substitutents go on for pages such as

R^1 is selected from:

(1) halogen,
(2) C_{1-6}alkyl,
(3) -CN,
(4) $-C(O)R^7$,
(5) $-OR^d$,
(6) $-NR^5R^6$,
(7) $-S(O)_2R^7$,
(8) cycloalkyl,
(9) cycloheteroalkyl,
(10) aryl, and
(11) heteroaryl,

wherein each alkyl moiety is unsubstituted or substituted with one, two, or three substituents independently selected from R^a, and each cycloalkyl, cycloheteroalkyl, aryl and heteroaryl moiety is unsubstituted or substituted with one, two, or three substituents independently selected from R^b;

R^2 is selected from:

(1) hydrogen,
(2) $-NR^5R^6$,
(3) $-C(O)R^7$,
(4) C_{1-6}alkyl,
(5) C_{2-6}alkenyl,
(6) C_{2-6}alkynyl,
(7) aryl,

(8) arylC$_{1-6}$alkyl-,

(9) arylC$_{2-6}$alkenyl-,

(10) heteroaryl,

(11) heteroarylC$_{1-6}$alkyl-,

(12) heteroarylC$_{2-6}$alkenyl-,

(13) cycloalkyl,

(14) cycloheteroalkyl-, and

(15) -OR^{d},

wherein each alkyl, alkenyl, and alkynyl moiety is unsubstituted or substituted with one, two, or three substituents independently selected from R^{a}; and each aryl and heteroaryl moiety is unsubstituted or substituted with one, two, or three substituents independently selected from R^{b}, and each cycloalkyl and cycloheteroalkyl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^{b} and oxo;

or R^{1} and R^{2} together form a 4 to 7 membered ring, containing 0, 1, or 2 heteroatoms independently selected from nitrogen, oxygen, and sulfur; unsubstituted or substituted on carbon or nitrogen with one, two or three substituents independently selected from R^{b}, wherein one or two of the carbon substituents may also be oxo, and wherein the ring is saturated or has one degree of unsaturation;

R^{3} is selected from:

(1) hydrogen,

(2) C$_{1-6}$alkyl,

(3) C$_{1-6}$alkyloxy-,

(4) trifluoromethyl,

(5) trifluoromethoxy-,

(6) halo, and

(7) C$_{3-7}$cycloalkyl,

wherein the alkyl moiety is unsubstituted or substituted with one, two, or three substituents independently selected from R^{a}, and the cycloalkyl moiety is unsubstituted or substituted with one to three substituents selected from R^{b} and oxo;

R^{4} is selected from:

(1) hydrogen, and

(2) -CH$_{2}$-R^{8};

R^{5} and R^{6} are each independently selected from:

(1) hydrogen,

(2) C$_{1-10}$alkyl,

(3) C$_{2-10}$alkenyl,

(4) C_{2-10}alkynyl,
(5) aryl,
(6) arylC_{1-4}alkyl-,
(7) heteroaryl,
(8) heteroarylC_{1-4}alkyl-,
(9) cycloalkyl,
(10) cycloalkylC_{1-4}alkyl-,
(11) trifluoromethyl,
(12) -C(O)-R^c,
(13) -CO_2R^c,
(14) -C(O)C(O)OR^c,
(15) -C(O)C(O)NR^dR^f,
(16) -$S(O)_mR^e$, and
(17) -C(O)$N(R^d)S(O)_mR^e$,

wherein each alkyl, alkenyl, alkynyl moiety is unsubstituted or substituted with one or two R^a substituents, and each cycloalkyl, heteroaryl and aryl moiety is unsubstituted or substituted with one or two R^b substituents,

or R^5 and R^6 together form =CH-$N(R^e)(R^f)$;

R^7 is selected from:

(1) hydrogen,
(2) C_{1-10}alkyl,
(3) C_{2-10}alkenyl,
(4) C_{2-10}alkynyl,
(5) cycloalkyl,
(6) cycloalkyl-C_{1-10}alkyl-,
(7) cycloheteroalkyl,
(8) cycloheteroalkyl-C_{1-10}alkyl-,
(9) aryl,
(10) heteroaryl,
(11) aryl-C_{1-10}alkyl-,
(12) heteroaryl-C_{1-10}alkyl-,
(13) -OR^c,
(14) -NR^dR^e,
(15) -NH(C=O)OR^e, and
(16) -$NR^dSO_2R^e$,

wherein each alkyl, alkenyl, and alkynyl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^a, and each cycloalkyl, cycloheteroalkyl, aryl and heteroaryl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^b;

R^8 is selected from:

(1) hydrogen,
(2) -$(CH_2)_nOC(O)R^c$,
(3) C_1-galkyl,
(4) C_2-galkenyl,
(5) C_2-galkynyl,
(6) cycloalkyl,
(7) cycloalkyl-C_1-galkyl-,
(8) cycloheteroalkyl,
(9) cycloheteroalkyl-C_1-galkyl-,
(10) aryl,
(11) heteroaryl,
(12) aryl-C_1-galkyl-, and
(13) heteroaryl-C_1-galkyl-,

wherein each alkyl, alkenyl, and alkynyl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^a, and each cycloalkyl, cycloheteroalkyl, aryl and heteroaryl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^b;

Ar^1 and Ar^2 are independently selected from:

(1) aryl,
(2) heteroaryl,

wherein each aryl and heteroaryl moiety is unsubstituted or substituted with one, two, three or four substituents independently selected from R^b;

each R^a is independently selected from:

(1) -OR^c,
(2) -$NR^dS(O)_mR^c$,
(3) -NO_2,
(4) halogen,
(5) -$S(O)_mR^c$,
(6) -SR^e,
(7) -$S(O)_2OR^e$,
(8) -$S(O)_mNR^eR^f$,

and on

and on. Claim 1 goes on for 10 pages.

2) The nature of the invention: The invention is a (highly) substituted compound that is useful to treat a disease mediated by cannabinoid receptors.

3) The state of the prior art:.

The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses a hydrogen changes the properties altogether. A good example is a theophylline verses caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

How to make :- It is not easy to synthesize compounds.
As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious)

....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

4) The level of one of ordinary skill: The ordinary artisan is highly skilled.

5) The level of predictability in the art: It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

6) The amount of direction provided by the inventor: The inventor provides very little direction in the instant specification. Examples of a limited scope of compounds have been made. Even though according to MPEP applicants do not have to enable each and every embodiment but atleast 50% should be enabled. In this case only about 2% has been enable.

7) The existence of working examples: The instant specification has a few examples as given above .

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are few working examples, and the unpredictability in the art is very high, the amount of experimentation is very high and burdensome and undue.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Conclusion

Claims 1-6 and 13 are rejected.

Claim 7 is objected to as containing non-elected subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

June 3, 2009